## REMARKS

Claims 34-42 and 64 are pending upon entry of this amendment. Claims 43-63 and 65-66 have been canceled. Claim 38 has been amended to specify the region of complementarity. Support is found in the specification at least at page 9, paragraph 43. No new matter has been introduced by the amendments.

Applicants thank the Examiner for notification that the drawings submitted on 20 September 2001 have been accepted and for acknowledgement of the priority claims.

### I. The Restriction Requirement

Applicants' election with traversal of the claims of Group I, *i.e.*, claims 34-63 directed to isolated polynucleotides, recombinant vectors, recombinant cells, and methods of making recombinant vectors, has been made final. However, claims 64-66 have been withdrawn from examination because they are directed to methods for detecting *E. coli.* Claims 34-42 of Group I and claim 64 of the detection method claims remain pending upon entry of this amendment. Since claims 34-42 and claim 64 are related as between a product and a process for using the product, and process claim 64 includes all the limitations of the product, the Examiner in any case would be obligated to rejoin claim 64 if the elected claims are found allowable. In light of the decisions in *In re Ochiai*, 71 F.3d 1565, 37 USPQ2d 1127 (Fed. Cir. 1995) and *In re Brouwer*, 77 F.3d 422, 37 USPQ 2d 1663 (Fed. Cir. 1996), a notice was published in the Official Gazette which set forth new guidelines for the treatment of product and process claims. *See* 1184 OG 86 (March 26, 1996). Specifically, the notice states that "in the case of an elected product claim, rejoinder will be permitted when a product claim is found allowable and the withdrawn process claim depends from or otherwise includes all the limitations of an allowed product claim." *Id.* Accordingly, Applicants respectfully request that if any of the claims of Group I are found allowable, claim 64 be rejoined and examined for patentability.

### II. Claim Rejections under 35 U.S.C. § 101

Claims 34-63 are rejected as allegedly lacking either a well-established utility or a specific, substantial, and credible utility. The rejection is respectfully traversed.

Initially, Applicants note that claims 43-63 have been canceled. The rejection will be discussed as it applies to the remaining claims.

The Examiner states that the claimed subject matter lacks both a specific asserted utility and a substantial "real world" utility.

> [T]he disclosed uses are generally applicable to broad classes of this subject matter. In addition, further characterization of the claimed subject matter would be required to identify or reasonably confirm a 'real world' use. The examiner does not find an adequate nexus between the disclosure of record and the asserted properties of the claimed subject matter.

Paper No. 6 at page 4, lines 5-8. Further, the Examiner has expressed concern that the biological activity of a polypeptide encoded by the claimed polynucleotides is uncertain if based on homology alone and not supported by data that demonstrate biological activity.

> [A]pplicant has identified a sequence which is known in the prior art and which has a stated sequence similarity to the claimed sequence. Absent factual biological activity data, one skilled in the art would have reason to doubt that sequence similarity alone would reasonably support the assertion that the biological activity of the claimed subject matter would be the same as that of the similar sequence.

Paper No. 6 at page 5, lines 2-7, emphasis added.

Even if, for the sake of argument, the specification failed to assert a biological activity for the claimed subject matter that would be readily accepted by one of skill in the art, the Examiner has not considered another asserted utility which is independent of any biological activity. The claimed polynucleotides can be used to detect the presence of pathogenic bacteria, especially the uropathogenic *E. coli* strain J96 from which the claimed open reading frame (ORF) was obtained. The use of polynucleotide sequences of the invention to generate hybridization probes and amplification primers to detect the presence of *E. coli* J96 in a sample is described, for example, at paragraphs 64 and 65 and in the section on diagnostic assays beginning at paragraph 106. This asserted use of the claimed ORF is specific, because the claimed polynucleotide sequences are unique to *E. coli* J96, and it is substantial because knowledge of a biological activity is not required for the asserted use to be carried out in a real world context.

Furthermore, Applicants believe that the assignment of biological activity in this case would be accepted as more likely than not true by one of skill in the art. The claimed ORF is 96% identical and 97% similar to a transposase identified in a plasmid of *Yersinia pestis*, a highly pathogenic microorganism. *See* Table 1 and Genbank U59875. Because transposases are common features of pathogenicity islands, the skilled artisan would

expect to find an ORF encoding a transposase or similar mobility-inducing enzyme in a pathogenicity island. *See, e.g.*, Hacker et al., Annu. Rev. Microbiol. 54:641-79 (2000), at 643 (attached as Exhibit A). In the present case, the skilled artisan would agree that the claimed ORF more likely than not does encode a transposase, based on the 96% sequence identity to the sequence disclosed in Genbank U59875 and location of the ORF in an *E. coli* pathogenicity island. Therefore, the examiner has not established a *prima facie* case that the asserted utility is not specific and substantial.

Thus, for the reasons discussed above, the withdrawal of this rejection is respectfully requested.

## III. Claim Rejections under 35 U.S.C. § 112, First Paragraph, Enablement

Claims 34-63 are rejected as allegedly lacking enablement. The rejection is respectfully traversed.

The Examiner asserts that the significance of the claimed sequence is undefined, and therefore the specification does not enable one of skill in the art to make or use the invention. Initially, Applicants point out that the specification clearly enables how to make the polynucleotide sequences of the instant claims. Applicants assume that the Examiner's rejection was actually directed toward use of the invention.

This rejection is based on the previously discussed rejection for alleged lack of utility. However, in light of the arguments presented above which demonstrate that the claimed polynucleotides and methods can be used to detect the presence of pathogenic *E. coli* bacteria and that the claimed ORF more likely than not has activity as a transposase, Applicants respectfully submit that this rejection is moot and should be withdrawn.

## IV. Claim Rejections under 35 U.S.C. § 112, First Paragraph, Written Description

Claims 35, 36, 40, and 42-63 are rejected as allegedly containing new matter and therefore lacking written description. The rejection is respectfully traversed.

Initially, Applicants note that claims 43-63 have been canceled. The rejection will be discussed as it applies to the remaining claims.

### A. New Matter Rejection for "heterologous polynucleotide sequence"

Claims 35 and 36 recite the phrase "heterologous polynucleotide sequence," which the Examiner considers to be new matter. Applicants respectfully disagree. In the instant

group of claims, the phrase "heterologous polynucleotide sequence" does not require definition in the specification because it is merely a term of art which is used with its ordinary meaning. At the time of the invention, a heterologous sequence was understood as simply a sequence that is different from a reference sequence and not derived from that reference sequence. For example, one author in a molecular biology reference book defines "heterologous sequences" as "nucleic acid sequences that are dissimilar and evolutionarily unrelated." M.M. Cox in *Molecular Biology and Biotechnology, A Comprehensive Desk Reference*, Ed. R.A. Meyers, Wiley-VCH, Inc, NY, 1995, at page 784 (attached as Exhibit B). Thus, with respect to the instant group of claims, a heterologous polynucleotide sequence is any nucleic acid sequence that is "dissimilar and evolutionarily unrelated to" the sequence of ORF ID 4 of CONTIG ID 65, represented by nucleotides 2889-1915 of SEQ ID NO:65. Thus, claims 35 and 36 do not introduce new matter with respect to the use of "heterologous polynucleotide sequence," and withdrawal of the rejection is respectfully requested.

**B. New Matter Rejection for "polynucleotide is operably associated"**

The recitation of "polynucleotide is operably associated" in claims 40 and 42 is also said to introduce new matter. Applicants respectfully disagree. The specification clearly contemplates heterologous regulatory sequences which can be operably linked (associated) with the polynucleotides of the invention.

> The present invention is directed to isolated nucleic acid fragments of the PAIs of *E. coli* J96. Such fragments include, but are not limited to, nucleic acid molecules encoding polypeptides (hereinafter open reading frames (ORFs)), nucleic acid molecules that modulate the expression of an operably linked ORF (hereinafter expression modulating fragments (EMFs)), and nucleic acid molecules that can be used to diagnose the presence of *E. coli* in a sample (hereinafter diagnostic fragments (DFs)).

Specification at page 8, paragraph 41. Heterologous regulatory sequences (or "expression modulating fragments") and their use are further described at page 13, paragraph 61; at page 15, paragraph 68; at page 46, paragraph 190; and elsewhere in the specification. Thus, it is respectfully submitted that the term "polynucleotide is operably associated" does not introduce new matter, and withdrawal of the rejection is requested.

**C. New Matter Rejection for Hybridization Conditions**

Claim 43, and claims 44-51 depending therefrom, are said to introduce new matter in the recitation of incubation "at 50-65°C" and washing in "0.5XSSC at 50-65°C". Applicants respectfully disagree that the recited language introduces new matter. However, these claims have been canceled, thereby rendering the rejection moot.

**D. New Matter Rejection for "at least"**

Claims 52, 61, and 62 each recite "at least" 15, 20, or 40 nucleotides, respectively, which is allegedly new matter given the teaching at page 12, paragraph 56, of "at least about" 15, 20, or 40 nucleotides. Applicants respectfully disagree that the recited language introduces new matter. However, these claims have been canceled, rendering the rejection moot.

## V. Claim Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 38, 40, 42, 43, 47, 49, 51, 56, 58, and 60 are rejected as allegedly being indefinite. The rejection is respectfully traversed.

Initially, Applicants note that claims 43, 47, 49, 51, 56, 58, and 60 have been canceled. The rejection will be discussed as it applies to the remaining claims.

**A. Alleged Indefiniteness of "operably associated"**

The term "operably associated" in claims 40 and 42 is said to be vague and indefinite because it is allegedly unclear which criteria are used to determine that a polynucleotide is "operably associated." Applicants respectfully disagree. The specification describes the operable association of a regulatory sequence to an ORF as follows:

> By 'expression modulating fragment' (EMF), is intended a series of nucleotides that modulate the expression of an operably linked ORF or EMF. A sequence is said to 'modulate the expression of an operably linked sequence' when the expression of the sequence is altered by the presence of the EMF.

Specification at page 13, paragraph 61. Thus, the criteria are defined functionally; operable association is achieved whenever "the expression of the sequence is altered by the presence of the EMF." Furthermore, several non-limiting examples of such operable association are provided throughout the specification. Thus, Applicants respectfully submit that the metes and bounds of the instant claims are clear and definite, and the rejection should be reconsidered and withdrawn.

**B. Alleged Indefiniteness of "sequence complementary"**

The use of "sequence complementary" in claim 38 is said to be unclear with respect to the criteria used to determine that a sequence is complementary. The Examiner appears to find uncertainty in the length of the region of complementarity required in order for a complementary sequence to fall within the instant claims. Applicants submit that the amendment to claim 38 has removed any such uncertainty and obviated the rejection. Therefore, withdrawal of the rejection is respectfully requested.

## VI. Claim Rejections under 35 U.S.C. § 102(e)

Claims 38, 43-51, and 56 are rejected as allegedly anticipated by Valenuela et al., U.S. Patent 5,814,478. The rejection is respectfully traversed.

Initially, Applicants note that claims 43-51 and 56 have been canceled. The rejection will be discussed as it applies to claim 38.

The Examiner has presented an alignment showing that portion of SEQ ID NO:31 of Valenuela et al. is complementary to nucleotides 2459-2465 of SEQ ID NO:65 of the instant case. Thus, according to the Examiner, Valenuela et al. disclose a nucleic acid sequence which is complementary over only seven contiguous nucleotides to ORF ID 4 of CONTIG ID 65.

Claim 38 as amended recites a nucleic acid sequence complementary to the entire nucleic acid sequence of ORF ID 4 of CONTIG ID 65, which is 975 nucleotides in length. Because Valenuela et al. disclose only seven contiguous nucleotides of the complement of ORF ID 4 of CONTIG ID 65, Valenuela et al. do not anticipate claim 38. Therefore, withdrawal of this rejection is respectfully requested.

## CONCLUSION

Applicants respectfully request that the above-made amendments and remarks be entered and made of record in the file history of the instant application. Applicants believe that this application is now in condition for allowance.

If there are any fees due in connection with the filing of this paper, please charge the fees to Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136, such an extension is requested and the fee should also be charged to Deposit Account No. 08-3425.

Respectfully submitted,

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Enclosures

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of:
Dillon et al.

Atty. Docket No. PB324D1

Application No.: 09/956,004

Group Art Unit: 1631

Filed: September 20, 2001

Examiner: Ly, C.

For: Nucleotide Sequence of *Escherichia coli* Pathogenicity Islands

## VERSION WITH MARKINGS TO SHOW CHANGES MADE

***In the Claims:***

The indicated claim is amended as follows:

38. (Once Amended) A nucleic acid sequence complementary to the entirety of the nucleotide sequence ~~polynucleotide~~ of claim 34.